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### Remarks/Arguments

In response to the Rejection mailed July 27, 2005, Applicants have amended claim 84 to highlight that the biological cells or microorganisms retain undenatured proteins, and present the following remarks.

Claim 16 was rejected under 35 USC 112, first paragraph as failing to comply with the written description requirement. Specifically, the examiner contends "Applicants do not disclose that the proteins are immobilized in or on different fibers without denaturing the proteins in the specification." This rejection is traversed.

From this statement, it appears the examiner has misunderstood the invention. Almost the entire specification is concerned with making a microarray wherein the proteins retain their native biological properties which for most proteins means they are undenatured. A microarray is used in a protein binding assay or other biological assay that usually requires the proteins to be not denatured. Antibodies are well known to lose their binding ability when denatured. Therefore, to be operable in an immunoassay, some variations (the claimed ones) on the microarray of the present invention require undenatured proteins.

The specification is replete with instructions to maintain biological activity of the proteins during immobilization. When discussing the different classes of fibers, the first class of fibers describes immobilization where "The temperature is chosen based on the solidifying properties of the matrix and the thermolabile properties of the agent of interest." The fifth class of fibers is described as having "Thus gels are available or can be produced which contain labile biomolecules without exposing them to denaturing temperatures." At risk of being redundant, a paragraph in the specification explains this as:

*In one embodiment, the microarrays are produced by diffusion and entrapment after polymerization of the strands. An element of a microarray is formed by preforming a polymeric strand, then incorporating a biological target molecule into the strand by a method including, but not limited to, diffusion from a solution containing the biological target molecule. Such a method of incorporating labile biological target molecules into polymeric avoids harsh conditions of polymerization, such as heat, presence of free radicals etc. that might alter a biological target molecule. Further, such a method envisages entrapping the*

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*biological target molecule within the polymeric strand while concomitantly preventing subsequent diffusion of the biological target molecule out of the strand.*

Accordingly, the language is well described in the specification and the rejection should be withdrawn.

Claims 16, 18, 22-24 and 81 were rejected under 35 USC 102(e) as being anticipated by Borrelli et al.

As pointed out previously, Borrelli et al uses different immobilization techniques of their "biological material" which are denaturing of proteins. Therefore Borrelli et al does not perform the claimed method. The examiner has not pointed to any embodiment that can immobilize proteins without denaturing them, a claimed feature.

The examiner contends that Borrelli et al disclose another embodiment "...where biomolecules are attached to beads which fit one at a time through the output of any individual channel..."

This particular embodiment of Borrelli et al does not even use proteins. Claim 16 (and 84) requires the immobilization of a protein. The "printing beads" taught have "biomolecules" which are either oligonucleotides or peptides. These "biomolecules" were synthesized in-vitro directly on the bead by conventional combinatorial synthesis, which uses denaturing organic solvents and other denaturing compounds.

Paragraph 7 of this rejection mentions claims 86 and 87 in a manner that does not relate to claim 86 and 87. Also claims 86 and 87 are not part of this rejection. Suspecting that these claims may be rejected under 35 USC 103 below, they are addressed below.

Therefore, the examiner has not shown any disclosure in Borrelli et al that suggests immobilizing proteins without denaturing them and thus the claimed invention is not taught. Accordingly, the rejection should be withdrawn.

Claims 84 and 85 were rejected under 35 USC 103 as being unpatentable over

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Borrelli et al in view of Walt et al and further in view of Attridge et al. Borrelli et al is cited to show the basic design with Walt teaching an array of living cells and Attridge et al teaching immobilizing antibodies on a capillary wall. From this the examiner concludes it obvious to immobilize cells or microorganisms in the capillaries of Borrelli et al. This rejection is respectfully traversed.

As noted above, Borrelli et al never uses any conditions, which would prevent denaturing the proteins. These claims recite the presence of biological cells or microorganisms, which of course contain proteins. To clarify matters, claim 84 has been amended to recite that those proteins are not denatured by the immobilizing process.

While the other references may not denature the proteins, those cells are not immobilized "in or on a length of different fibers" as claimed. To combine these references would be to use biological cells or microorganisms in place of "biomolecules" in Borrelli et al. When doing so, one results with denatured proteins and the same situation as given above in the rejection under 35 USC 102 above. Accordingly, for the reasons given in the reply to that rejection also, the rejection should be withdrawn.

Claims 86 and 87 were not included in this rejection, probably by typographical error, but appear intended to be rejected somehow.

Claim 86 recites fibers with "different concentrations of the same agent on different fibers". This aspect is not taught by the references. The examiner contends that Borrelli teaches that "each channel may have between 2 and 10  $\mu$ l of printable liquid, ... therefore the concentration between any two channels in the array would indeed vary." Having a different quantity of liquid is not a different concentration. It merely indicates a longer or larger bore hollow fiber. The claims recite different concentrations of protein in the fiber. This distinction is important for the eventual use for the microarray as a quantitative assay device rather than merely a qualitative one.

Claims 16-18, 81, 84 and 85 were rejected under the doctrine of obviousness-type double patenting over claims 1-17 of U.S. Patent 6,713,309. Applicants request this

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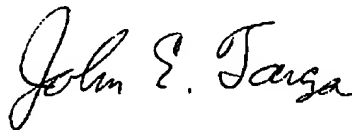
rejection be delayed until the claims have been indicated otherwise patentable. A terminal disclaimer may be filed at that time, as needed depending on the claim language otherwise allowable.

Applicants thank the examiner for recognizing that claims 82 and 83 are allowable.

In view of the amendments and comments above, the rejections other than obviousness-type double patenting have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowable claims are respectfully requested. If any issues remain, the examiner is encouraged to telephone the undersigned. Should only the obviousness-type double patenting rejection remain, please call the undersigned for a promptly filed terminal disclaimer.

If needed, applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,



Date: November 28, 2005

John E. Tarcza  
Reg. No. 33,638

Attachment: Petition for a one-month extension of time.

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